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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/768,917 | 01/24/2001 | Alain P. Vicari | SF0896K | 5028 |

24265 7590 11/02/2004

SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
2000 GALLOPING HILL ROAD
KENILWORTH, NJ 07033-0530

| EXAMINER |
|---|
| WEHBE, ANNE MARIE SABRINA |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | |

DATE MAILED: 11/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/768,917 | VICARI ET AL. | |
| | Examiner | Art Unit | |
| | Anne Marie S. Wehbe | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *8/13/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *21-24,27,29,31,33,35,36 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24,27,29,31,33,35,36 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's amendment and arguments filed on 8/13/04 have been entered. The declaration under 37 C.F.R. 1.131 also received on 8/13/04 has been entered. Claims 21-24, 27, 29, 31, 33, 35-36, and 69 are currently pending and under examination in instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

### *Priority*

As noted in previous office actions, the instant application was filed more than twelve months after the filing date of foreign application EP 0 974 357, filed on 7/16/98. Thus, priority to EP 0 974 357 has been denied. The effective priority date of the application is the actual filing date of instant application, 1/24/01.

### *Claim Rejections - 35 USC § 102*

The rejection of claims 21-24, 27, 29, 31, 33, 35-36, and 69 under 35 U.S.C. 102(e) as being anticipated by US 2002/0071825 A1 (6/13/02), hereafter referred to as Schall et al. is withdrawn in view of applicant's declaration under 37 CFR 1.131 which establishes that the inventors were in possession of the invention prior to April 21, 2000.

***Claim Rejections - 35 USC § 103***

The rejection of claims 21-24, 27, 29, 31, 33, 35-36, and 69 under 35 U.S.C. 103(a) as being unpatentable over EP 0 974 357 A1 (7/16/98), hereafter referred to as Caux et al., in view of WO 98/14573 (4/9/98), hereafter referred to as Luster et al., and Dieu-Nosjean et al. (1999) J. Leuk. Biol. Vol. 66, 252-262, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant rejection of record for reasons of record discussed in detail below.

As noted in previous office actions, while the EP 0 974 357 A1 document no longer qualifies as prior art under 102(a) regarding subject matter relating to MCP-4, this document does qualify as prior art in regards to the teachings contained therein relating to other chemokines such as MIP-3α, RANTES, and MIP-1α.

The claims as amended recite methods for enhancing a humoral immune response in a mammal comprising administering MCP-4 and an antigen to said mammal wherein the antigen and MCP-4 are not a fusion protein. The limitation that the methods enhance a humoral immune response is new. However, the rejection of record still applies. As discussed in detail in previous office actions, Caux et al. teaches methods of using chemokines such as MIP-3α, RANTES, and MIP-1α in combination with antigens for directing the migration of antigen presenting cells, including dendritic cells, to lymphoid organs in vivo in order to increase immune responses (Caux et al., columns 4-6, and 18-19). Luster et al. and Dieu-Nosjean et al. were cited to provide teachings and motivation for substituting MCP-4 for MIP-3α in the methods of Caux et al. While the office acknowledges that none of these references specifically refers to humoral immune

responses, both Luster et al. and Dieu-Nosjean et al. clearly teach that MCP-4 acts as an immune adjuvant by recruiting and activating dendritic cells. At the time of filing the activities of activated dendritic cells were well known, and included the regulation of humoral responses through the activation of B cells (see for instance, Fayette et al. (1998) Scand. J. Immunol., Vol. 48, 563-570). Thus, based on the known activities of activated dendritic cells, which includes activation of humoral immune responses, and the teachings of Luster et al. and Dieu-Nosjean et al. that MCP-4 recruits and activates dendritic cells, the skilled artisan would have had a reasonable expectation of success in enhancing humoral immune responses by administering MCP-4 and an antigen according to the teachings of Caux et al., Luster et al., and Dieu-Nosjean et al.

The applicant argues that the declaration previously submitted under 37 CFR 1.132 by Alain P. Vicari et al. demonstrates that hMCP-4 injection increases the antigen specific humoral responses following DNA immunization, whereas hMIP-3α does not, and thus the increased results observed with MCP-4 would not have been expected based on the results obtained using MIP-3α. The previous office addressed the declaratory evidence in detail. As stated in the previous office action, Exhibit A of the 132 declaration shows that MCP-4 appears to generate increased levels of total IgG as compared to MIP-3α. In the declaration, Dr. Vicari states that the skilled artisan would not have expected MCP-4 to increase antibody responses to antigen based on the activity of MIP-3α. The previous office further states that the MPEP in section 716.02(d) states that in the consideration of evidence of unexpected results, "Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the 'objective evidence of nonobviousness must be commensurate in scope with the

claims which the evidence is offered to support.'", citing *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) (see also *In re Peterson*, 315 F. 3e 1325, 1329-31, 65 USPQ2d 1379, 1382-85 (Fed. Cir. 2003), and *In re Grasselli* 713 F.2d 731, 741, 218 USPQ 769, 777 (Fed. Cir. 1983)). In the instant case, the evidence provided to demonstrate "unexpected results" and thus non-obviousness is not commensurate in scope with the claims as written. The evidence provided discloses results from experiments where protein MCP-4 is administered three hours before the administration of a plasmid vector encoding the target antigen, β-galactosidase, resulting in the generation of IgG antibody generation. However, the claims are not so limited and read broadly on the simultaneous or sequential administration of MCP-4 and antigen, and further read on administering MCP-4 in the form of a nucleic acid or protein, and administering antigen in the form of nucleic acid or protein. It is unclear from the data provided whether the increase in IgG observed by applicants in the declaratory experiments would occur if MCP-4 were administered in the form of a nucleic acid, or where MCP-4 were co-administered with the antigen or administered subsequent to antigen administration. Thus, while the applicant's results demonstrate unexpected results in obtaining higher levels of antibodies following sequential administration of MCP-4 protein followed by administration of a nucleic acid encoding an antigen, the results are not commensurate in scope with the scope of the claims as written.

Therefore, the rejection of record stands.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, the technology center fax number is (703) 872-9306. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER